Mutation and location important in cancer treatment

Targeting drugs to mutations in cancer cells is a powerful application of precision medicine, but the histology approach should not be abandoned, according to findings published in The New England Journal of Medicine.

In a phase 2 “basket” trial, David Hyman (Memorial Sloan Kettering Cancer Center, New York, NY, USA) and colleagues tested the oral kinase inhibitor vemurafenib in cancers other than melanoma, for which this drug is mainly used. “It’s a very interesting trial because it is one of the first to explore many malignancies for specific mutations captured in a ‘molecular basket’”, says Arturo Loaiza-Bonilla (University of Pennsylvania, Philadelphia, PA, USA). The tumors of the 122 enrolled patients had the V600 mutation in the BRAF gene, which is associated with aggressive disease. 89% of participants had previous cancer treatment.

Results for non-small-cell lung cancer were most striking. Eight (42%, 95% CI 20–67) of 19 assessed patients had partial responses. Median progression-free survival was 7.3 months (95% CI 3.5–10.8) and preliminary 12-month overall survival was 66% (95% CI 36–85). For the rare Erdheim–Chester disease, the first patient to enroll was on her way to the hospice, unable to walk. “2 weeks later she came back, walking and feeling fine. She’s been asymptomatic for over a year”, corresponding author José Baselga (Memorial Sloan Kettering Cancer Centre, New York, NY, USA) says. The researchers discovered that some patients with colon cancer with a BRAF mutation responded if they also took an epidermal growth factor receptor inhibitor (cetuximab). But for other cancers, only a few patients responded. “What we’ve learned is that the driver mutation matters, but the tissue of origin is also important”, says Baselga.

Edward McKenna from Genentech (South San Francisco, CA, USA), the drug manufacturer, cautioned that the study was not meant to influence cancer treatment. “It’s important to differentiate between selecting treatment by mutation in the investigational setting, as in basket studies, and use as a tool to select treatment for patients in the clinical setting.”

Baselga foresees combining conventional drugs, targeted treatments, and immunotherapies, and offering genetic testing earlier in the treatment process. Kenna Mills Shaw (MD Anderson Institute for Personalized Cancer Therapy, Houston, TX) agrees. “Often patients are undergoing genetic testing at the end of treatment, on a sample that has evolved through lines of therapy.”

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